

We claim:

1. A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder, said method comprising detecting a marker that is linked to map position 4q35.2 of the human genome in a sample derived from a subject, wherein the detection is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.
2. The method according to claim 1 wherein the marker linked to map position 4q35.2 is located between or comprises the microsatellite markers selected from the group consisting of:
 - (i) the microsatellite marker designated D4S1164 (SEQ ID NO: 21) and the microsatellite marker D4S1192 (SEQ ID NO: 27);
 - (ii) the microsatellite marker designated D4S910 (SEQ ID NO: 22) and the microsatellite marker D4S1374 (SEQ ID NO: 28);
 - (iii) the microsatellite marker designated D4S3173 (SEQ ID NO: 23) and the microsatellite marker D4S1375 (SEQ ID NO: 29);
 - (iv) the microsatellite marker designated D4S3236 (SEQ ID NO: 24) and the microsatellite marker designated D4S3051 (SEQ ID NO: 30); and
 - (v) the microsatellite marker designated D4S2827 (SEQ ID NO: 25) and the microsatellite marker D4S2643 (SEQ ID NO: 31).
3. The method according to claim 1 wherein the marker linked to map position 4q35.2 is located within or comprises the FAT gene.
4. A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder, said method comprising detecting a marker within a FAT gene or an expression product thereof that is associated with a bipolar affective disorder in a sample derived from a subject, wherein a presence of the marker is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.
5. The method according to claim 4 wherein the FAT gene comprises a nucleotide sequence selected from the group consisting of:
 - (i) a nucleotide sequence at least 80% identical to the nucleotide sequence set forth in SEQ ID NO: 1;

- (ii) a nucleotide sequence that encodes a mRNA at least 80% identical to the nucleotide sequence set forth in SEQ ID NO: 2 or 4; and
- (iii) a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 3 or 5.
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6. The method according to claim 4 wherein the marker is located within the 3' region of the FAT gene.
- 10 7. The method according to claim 3 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 139,260 to nucleotide position 170,001 of SEQ ID NO: 1.
- 15 8. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 146,012 to nucleotide position 170,001 of SEQ ID NO: 1.
- 20 9. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,108 to nucleotide position 170,001 of SEQ ID NO: 1.
- 25 10. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,199 to nucleotide position 170,001 of SEQ ID NO: 1.
- 30 11. The method according to claim 6 wherein the 3' region of the FAT gene comprises or consists of nucleic acid comprising a nucleotide sequence corresponding to the region spanning from nucleotide position 148,333 to nucleotide position 170,001 of SEQ ID NO: 1.
- 35 12. The method according to claim 4 wherein the marker comprises a polymorphism in the FAT gene.

13. The method according to claim 12 wherein the polymorphism is a single nucleotide polymorphism (SNP).
- 5 14. The method according to claim 13 wherein the SNP is selected from the group consisting of a cytosine at a position corresponding to nucleotide 80,217 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 130,625 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 130,613 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 142,199 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 142,460 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 145,782 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,008 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,199 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,333 of SEQ ID NO: 1, a thymine at position 148,333 of SEQ ID NO: 1, a cytosine at a position corresponding to 148,333 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 151,403 of SEQ ID NO: 1 and a thymine at a position corresponding to nucleotide 153,127 of SEQ ID NO: 1.
- 15 15. The method according to claim 13 wherein the SNP is selected from the group consisting of a guanine at a position corresponding to nucleotide 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to nucleotide 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, a cytosine at a position corresponding to nucleotide 148,108 of SEQ ID NO: 1, an adenine at a position corresponding to nucleotide 148,333 of SEQ ID NO: 1 and a thymine at position 148,333 of SEQ ID NO: 1.
- 30 16. The method according to claim 13 wherein the subject does not have a family history of psychiatric illness and the SNP is selected from the group consisting
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of a guanine at a position corresponding to 139,968 of SEQ ID NO: 1, a guanine at a position corresponding to 146,012 of SEQ ID NO: 1, a thymine at a position corresponding to 148,108 of SEQ ID NO: 1 and a thymine at a position corresponding to 148,333 of SEQ ID NO: 1.

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17. The method according to claim 13 wherein the subject has a family history of psychiatric illness and the SNP is selected from the group consisting of a thymine at a position corresponding to 139,968 of SEQ ID NO: 1, an adenine at a position corresponding to 146,012 of SEQ ID NO: 1, a cytosine at a position corresponding to 148,108 of SEQ ID NO: 1 and a cytosine at a position corresponding to 148,333 of SEQ ID NO: 1.
18. The method according to claim 4 wherein the marker comprises a nucleic acid comprising a nucleotide sequence at least about 80% identical to at least about 20 contiguous nucleotides in a sequence selected from the group consisting of:
 - (i) a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 4;
 - (ii) a sequence capable of encoding a polypeptide comprising an amino acid sequence at least 80% homologous to the sequence set forth in SEQ ID NO: 3 and SEQ ID NO: 5; and
 - (iii) a sequence complementary to a sequence set forth in (i) or (ii).
19. The method according to claim 4 wherein the marker is detected by hybridising a nucleic acid probe or primer comprising the sequence of the marker to a marker linked to nucleic acid in a biological sample derived from a subject under moderate to high stringency hybridisation conditions and detecting the hybridisation using a detection means, wherein hybridisation of the probe to the sample nucleic acid indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.
20. The method according to claim 4 wherein the marker is detected by hybridising a nucleic acid probe or primer comprising the sequence of the marker to a nucleic acid that is linked to the marker in nucleic acid in a biological sample derived from a subject under moderate to high stringency hybridisation conditions and detecting the hybridisation by a detection means, wherein

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hybridisation of the probe to the sample nucleic acid indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.

21. The method according to claim 19 or 20 wherein the detection means is a nucleic acid hybridisation reaction or a nucleic acid amplification reaction.
22. The method according to claim 21 wherein the detection means is a polymerase chain reaction.
23. The method according to claim 19 or 20 wherein the nucleic acid probe or primer comprises a sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.
24. The method according to claim 4 wherein the marker is detected by contacting a biological sample derived from the subject with an antibody capable of specifically binding to said marker for a time and under conditions sufficient for an antibody-ligand complex to form and then detecting the complex wherein detection of the complex indicates that the subject being tested is predisposed to or suffers from a bipolar affective disorder.
25. The method according to claim 4 wherein the biological sample comprises a nucleated cell.
26. The method according to claim 25 wherein the biological sample is selected from the group consisting of whole blood, serum, plasma, peripheral blood mononuclear cells (PBMC), a buffy coat fraction, saliva, urine, a buccal cell and a skin cell.
27. The method according to claim 25 wherein the biological sample comprises a cell or cell extract or mixture thereof derived from a tissue selected from the group consisting of a brain, a spinal cord, skin, a lung, a kidney and a pancreas

28. The method according to claim 25 wherein the biological sample comprises a cell or an extract thereof or a mixture thereof isolated using a method selected from the group consisting of aminocentesis, chorionic villus sampling, fetal blood sampling and fetal skin biopsy.
29. The method according to any one of claims 25 to 28 wherein the biological sample has been derived previously from the subject.
30. A method for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder in a subject, said method comprising:
- (i) amplifying nucleic acid from the subject using an amplification reaction, wherein the amplification reaction is performed using a pair of primers selected from the group consisting of:
- (a) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 32 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 33;
- (b) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 34 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 35;
- (c) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 36 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 37;
- (d) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 38 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 39;
- (e) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 40 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 41;
- (f) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 42 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 43;
- (g) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 44 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 45;

- (h) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 46 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 47;
- 5 (i) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 48 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 49;
- (j) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 50 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 51;
- 10 (k) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 53 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 54; and
- (l) a primer comprising the nucleotide sequence set forth in SEQ ID NO: 56 and a primer comprising the nucleotide sequence set forth in SEQ ID NO: 57;
- 15 (ii) detecting a polymorphism in the amplified nucleic acid from (i), wherein said polymorphism is indicative of a bipolar affective disorder or a predisposition to a bipolar affective disorder in the subject.
- 20 31. The method according to claim 30 wherein the polymorphism is detected by determining the nucleotide sequence of the amplified nucleic acid.
32. Use of a probe or primer comprising at least about 20 nucleotides that is capable of selectively hybridizing to the sequence set forth in SEQ ID NO: 1 and detecting a marker in a FAT gene that is associated with a bipolar affective disorder or a predisposition to a bipolar affective disorder in the manufacture of a diagnostic reagent for determining a predisposition of a subject to a bipolar affective disorder or diagnosing a bipolar affective disorder.
- 25 33. The use according to claim 32 wherein the probe or primer comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID
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NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.

34. A probe or primer comprising at least about 20 nucleotides that is capable of selectively hybridizing to the sequence set forth in SEQ ID NO: 1 and detecting a marker in a FAT gene that is associated with a bipolar affective disorder or a predisposition to a bipolar affective disorder.
35. The probe or primer according to claim 34 comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57 and SEQ ID NO: 58.
36. A method for determining a subject that carries a gene or allele of a gene or a polymorphism that is associated with a bipolar affective disorder comprising detecting a marker within a FAT gene that is associated with a bipolar affective disorder in a sample derived from the subject, wherein detection of said marker indicates that the subject is a carrier of a gene or allele of a gene or a polymorphism is associated with a bipolar affective disorder.
37. A method of treatment or prophylaxis of a bipolar affective disorder comprising:
- (i) performing the method of any one of claims 1 to 31 for determining a bipolar affective disorder or a predisposition to a bipolar affective disorder; and
 - (ii) administering or recommending a therapeutic for the treatment of bipolar affective disorder.
38. A method for identifying a marker that is associated with a bipolar affective disorder, said method comprising:
- (i) identifying a polymorphism or allele within a FAT gene or an expression product thereof;

- (ii) analyzing a panel of subjects to determine those that suffer from a bipolar affective disorder, wherein not all members of the panel comprise the polymorphism or allele; and
- (iii) determining the variation in the development of a bipolar affective disorder wherein said variation indicates that the polymorphism or allele is associated with a subject's predisposition to a bipolar affective disorder.
39. A method for determining a candidate compound for the treatment of a bipolar affective disorder comprising:
- (i) administering a candidate compound to an animal or cell comprising or expressing a marker within a FAT gene that is associated with a bipolar affective disorder and determining the level of FAT expression in said cell or animal;
- (ii) administering a candidate compound to an animal or cell that does not comprise or express a marker within a FAT gene that is associated with a bipolar affective disorder and determining the level of FAT expression in said cell or animal; and
- (iii) comparing the level of FAT expression at (i) and (ii), wherein a decreased level of FAT expression at (i) relative to (ii) indicates that the compound is a candidate compound for the treatment of a bipolar affective disorder.
40. A method for determining a candidate compound for the treatment of a bipolar affective disorder comprising:
- (i) administering a candidate compound to an animal or cell capable of expressing a FAT gene and determining the level of FAT expression in said cell or animal;
- (ii) determining the level of FAT expression in an animal or cell capable of expressing a FAT gene in the absence of the candidate compound; and
- (iii) comparing the level of FAT expression at (i) and (ii), wherein a decreased level of FAT expression at (i) relative to (ii) indicates that the compound is a candidate compound for the treatment of a bipolar affective disorder.
41. The method according to claim 39 or 40 wherein the level of FAT expression is determined by determining the level of FAT mRNA in the cell or animal.

42. A process for identifying or determining a compound or modulator for the treatment of a bipolar affective disorder said method comprising:
- 5 (i) performing the method according to any one of claims 39 to 41 to thereby identify or determine a compound for the treatment of a bipolar affective disorder;
- (ii) optionally, determining the structure of the compound;
- (iii) optionally, providing the name or structure of the compound; and
- 10 (iv) providing the compound.
43. A process of manufacturing a compound for the treatment of a bipolar affective disorder comprising:
- (i) determining a candidate compound for the treatment of a bipolar affective disorder by performing the method according to any one of claims 39 to
- 15 41; and
- (ii) using the compound in the manufacture of a therapeutic or prophylactic for the treatment of bipolar affective disorder.